The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A compound having the formula I:

$$Y \xrightarrow{X} \bigvee_{N = 1 \atop W}^{R_1} R_2$$
(I)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C₁-C₆-alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_{2}$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and

wherein R^{1x} , R^{2x} , and R^{3x} are selected from the group consisting of

- (a) H
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,

- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) -OR^{1t}, and
- (6) $-NHR^{1t}$,

wherein R^{1t} is H or C_1 - C_6 -alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

$$R^{4w} = \begin{bmatrix} \\ N \\ Z \end{bmatrix}$$

wherein R^{1w} and R^{2w} are selected from the group consisting of

(a) H

(3)

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- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are not both H;

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Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^z$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_2-$,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and r is 0, 1, or 2;

with the proviso that when X is O, then Y is substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted heterocyclyl,

with the proviso that when W is morpholino, thiomorpholino, 1-oxido-thiomorpholino, 1,1-dioxido morpholino, piperazino, or N-substituted piperazino, R₂ is morpholino, thiomorpholino, 1-oxido-thiomorpholino, 1,1-dioxido-thiomorpholino, piperazino, or N'-[acetyl(alkanoyl of 1 to 3 carbon atoms)]piperazino, and X is NH, then Y is not hydrogen, alkyl of 1 to 3 carbon atoms, cyclohexyl, phenyl, chloro-phenyl, carboxy-phenyl, carbomethoxy-phenyl, or pyridyl;

with the proviso that when W is morpholino, thiomorpholino, 1-oxido-thiomorpholino, 1,1-dioxido morpholino, piperazino, or N-substituted piperazino, R₂ is morpholino, thiomorpholino, 1-oxido-thiomorpholino, 1,1-dioxido-thiomorpholino, piperazino, or N'-[acetyl(alkanoyl of 1 to 3 carbon atoms)]piperazino, and X is a direct link, then Y is not phenyl, substituted or unsubstituted C1-C6-alkyl, or 1-oxidothiomorpholino; and

with the proviso that when R₂ is phenyl independently substituted with one to five substituents selected from hydrogen, cycloalkyl, heterocycloalkyl, halo, nitro, amino,

sulphonamido, or alkylsulphonylamino, R_1 is hydrogen, haloalkyl, alkyl, or halo, and X is NR^{1x} , then Y is substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocyclyl.

2. The compound of claim 1, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted aryl,
- (3) substituted or unsubstituted heterocyclyl, and
- (4) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$; and

W is selected from the group consisting of

$$R^{4w}$$
 Z

wherein Z is -O- or -NRz-, wherein R^{4w} is H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$.

3. The compound of claim 1, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted heterocyclyl,
- (2) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,

(3)
$$-(CH_2)_m$$
- $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and
(4) ,

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$; and

W is selected from the group consisting of

$$R^{4w}$$
 Z

wherein Z is -O- or -NRz-, wherein R^{4w} is H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$.

4. The compound of claim 1, wherein

Y is substituted or unsubstituted aryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$; and

W is selected from the group consisting of

$$R^{4w}$$

wherein Z is -O- or -NRz-, wherein R^{4w} is H or substituted or unsubstituted $C_1\text{-}C_6\text{-alkyl}$.

5. The compound of claim 1, wherein

Y is substituted or unsubstituted alkyl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl; and

W is selected from the group consisting of

$$R^{4w}$$
 Z

wherein Z is -O- or -NRz-, wherein R^{4w} is H or substituted or unsubstituted C_1 - C_6 -alkyl.

6. The compound of claim 1, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted heterocyclyl,
- (2) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl;

R₂ is substituted or unsubstituted aryl; and

W is



wherein Z is -O- or -NH-.

7. The compound of claim 1, wherein

Y is substituted or unsubstituted aryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl;

R₂ is substituted or unsubstituted aryl; and

W is



wherein Z is -O- or -NH-.

8. The compound of claim 1, wherein

Y is substituted or unsubstituted alkyl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

wherein R^{1x} , R^{2x} , R^{3x} are independently H or substituted or unsubstituted C_1 - C_6 -alkyl;

R₂ is substituted or unsubstituted aryl; and

W is

wherein Z is -O- or -NH-.

9. The compound of claim 1, having the formula II:

$$Y \xrightarrow{X} \xrightarrow{R_1} R_2$$

$$X \xrightarrow{N} N$$

wherein Y is selected from the group consisting of

- (1) substituted or unsubstituted C₁-C₆-alkyl,
- (2) substituted or unsubstituted aryl,
- (3) substituted or unsubstituted heterocyclyl, and
- (4) substituted or unsubstituted heteroaryl; and

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -, and

10. The compound of claim 1, having the formula II:

$$Y \xrightarrow{X} \xrightarrow{R_1} R_2$$

$$X \xrightarrow{N} N$$

wherein Y and X, taken together, are selected from the group consisting of

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11. The compound of claim 1, having the formula II:

wherein Y and X, taken together, are selected from the group consisting of

12. The compound of claim 1, having the formula II:

wherein, Y and X, taken together, are selected from the group consisting of

$$H_{3}$$
C H_{3} CO H_{3} H_{3} CO H_{3} H_{2}

13. The compound of claim 1, having the formula III:

$$\begin{array}{c|cccc}
R_5 & R_6 & H & R_1 \\
\hline
N & & & & & \\
N & & & & & \\
N & & & & & \\
R_4 & & & & & \\
\end{array}$$
(III)

wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) $-COORt^1$,
- (4) $-COONH_2$,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t.}

14. The compound of claim 1, having the formula IV:

wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) $-COOR^{1t}$,
- (4) $-COONH_2$,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t}.

15. The compound of claim 1, having the formula V:

wherein R₃, R₄, R₅, R₆ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) -COOR^{1t},
- (4) $-COONH_2$,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t}; and

 R^{2a} and R^{2b} are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) halo,
- (4) $-(CH_2)_q-N(R^{2c}, R^{2d}),$
- (5) $-(CH_2)_q-N(R^{2c}, R^{2d})COR^{2e}$,
- (6) $-(CH_2)_q$ -OR^{2e},
- (7) $-(CH_2)_q$ -OCOR^{2e},
- (8) $-(CH_2)_q$ -OCOOR^{2e},
- (9) $-(CH_2)_q$ -COOR^{2e},
- (10) $-(CH_2)_q$ -CONR^{2c},
- (11) -CN,
- (12) $-NO_2$,
- (13) $-SO_2NH_2$,
- (14) -NHSO₂CH₃, and
- (15) $-SO_2R^{2f}$,

wherein R^{2c}, R^{2d}, R^{2e}, and R^{2f} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted phenyl; and q is 0, 1, 2, 3, or 4.
- 16. The compound of claim 1, having the formula VI:

$$\begin{array}{c|c}
 & H \\
 & N \\
 & N \\
 & N \\
 & N \\
 & N
\end{array}$$
(VI)

wherein R₂ is selected from the group consisting of

17. The compound of claim 1, having the formula VII:

$$R_9 \xrightarrow[R_8]{R_{10}} H \xrightarrow[N]{R_1} R_2$$

(VII)

wherein R₇, R₈, R₉, and R₁₀ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) $-COOR^{1t}$,
- (4) $-COONH_2$,
- (5) $-OR^{1t}$, and
- (6) $-NHR^{1t}$.

18. The compound of claim 1, having the formula VIII:

$$\begin{array}{c|c}
R_{10} & H & R_{1} \\
N & N & N \\
R_{9} & R_{7} & N & N
\end{array}$$

. (VIII)

wherein R₇, R₈, R₉, R₁₀ are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) $-COOR^{1t}$,
- (4) $-CONH_2$,
- (5) $-OR^{1t}$, and
- (6) $-NHR^{1t}$.

19. The compound of claim 1, having the formula IX:

$$\begin{array}{c}
H \\
N \\
N \\
N \\
N
\end{array}$$

$$\begin{array}{c}
\Pi \\
N \\
N
\end{array}$$

wherein R1a and R1b are selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) halo,
- (4) $-(CH_2)_q-N(R^{2c}, R^{2d}),$
- (5) $-(CH_2)_q$ -N(R^{2c}, R^{2d})COR^{2e},
- (6) $-(CH_2)_q$ -OR^{2e},
- (7) $-(CH_2)_q$ -OCOR^{2e},
- (8) $-(CH_2)_q$ -OCOOR^{2e},
- (9) $-(CH_2)_q$ -COOR^{2e},
- (10) $-(CH_2)_q$ -CONR^{2c},
- (11) -CN,
- (12) -NO₂,
- (13) $-SO_2NH_2$,
- (14) -NHSO₂CH₃, and
- (15) $-SO_2R^{2f}$,

wherein R^{2c}, R^{2d}, R^{2e}, and R^{2f} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted phenyl; and

wherein R₇ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,

- (3) $-COOR^{1t}$,
- (4) –CONH₂,
- (5) $-OR^{1t}$, and
- (6) $-NHR^{1t}$.
- 20. The compound of claim 1, having the formula X:

$$\begin{array}{c}
H \\
N \\
N \\
N \\
N
\end{array}$$

$$\begin{array}{c}
R_2 \\
N \\
N
\end{array}$$

$$\begin{array}{c}
(X)
\end{array}$$

wherein R₂ is selected from the group consisting of

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21. The compound of claim 1, having the formula XI:

wherein R^{2g} is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) $-CONHR^{2h}$,
- (4) $-CON(R^{2h})-(CH_2)_{2-3}-N(R^{2h}, R^{2i}),$
- (5) $-COR^{2j}$,
- (6) $-CO_2R^{2j}$,
- (7) $-COC_1-C_6$ -alkyl- CO_2H ,
- (8) $-CH_2-OC(=O)R^{2i}$,
- (9) $-CH_2-OC(=O)NHCHR^{2i}CO_2R^{2j}$,
- (10) $-P(=O)(OR^{2k}, OR^{2p}),$

(11)
$$OH$$
 , and OH , OH ,

wherein R^{2h}, R²ⁱ, R^{2j}, R^{2k}, and R^{2p} are selected from the group consisting

of

- (a) H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted aryl.

22. The compound of claim 1, having the formula XII:

wherein R^{2g} is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted alkyl,
- (3) $-CONHR^{2h}$,
- (4) $-CON(R^{2h})-(CH_2)_{2-3}-N(R^{2h}, R^{2i}),$
- (5) $-COR^{2j}$,
- (6) $-CO_2R^{2j}$,
- (7) $-COC_1-C_6$ -alkyl- CO_2H ,
- (8) $-CH_2-OC(=O)R^{2i}$,
- (9) $-CH_2-OC(=O)NHCHR^{2i}CO_2R^{2j}$,
- (10) -P(=O)(OR 2k , OR 2p), CO $_2$ H

wherein R^{2h}, R²ⁱ, R^{2j}, R^{2k}, and R^{2p} are selected from the group consisting of

- (a) · H,
- (b) substituted or unsubstituted alkyl, and
- (c) substituted or unsubstituted aryl.

23. A composition, comprising a pharmaceutically acceptable carrier and an amount of a compound effective to inhibit phosphotidylinositol (PI) 3-kinase activity in a human or animal subject when administered thereto, wherein the compound has the formula I:

$$Y \xrightarrow{X} \xrightarrow{R_1} R_2$$

$$X \xrightarrow{N} X$$

$$W$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_{2}$
- (8) $-C(R^{2x}, R^{3x})$ -, and

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

(a) H,

- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C2-C6-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

$$R^{4w}$$
 \subset \sum_{Z}^{N} \subset $(CH_2)r$

wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and

R²w are not both H;

(3)

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^z$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.

- 24. The composition of Claim 23 further comprising at least one additional agent for the treatment of cancer.
- 25. The composition of Claim 24, wherein the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.
- 26. A method for treating a condition by modulation of phosphotidylinositol (PI) 3-kinase activity comprising administering to a human or animal subject in need of such treatment an effective amount of a compound having the formula I:

$$Y \xrightarrow{X} \bigvee_{N = N}^{R_1} R_2$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and

wherein R^{1x} , R^{2x} , and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,

(g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

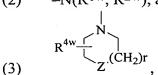
wherein R^{1t} is H or C₁-C₆-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and



wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{lw} and

R²w are not both H;

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^{z}$ -,
- (c) -S-,
- (d) -SO-,

- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.

- 27. The method of Claim 26, wherein the compound has an IC50 value of less than about 20 μ M in a cell proliferation assay.
 - 28. The method of Claim 26, wherein the condition is cancer.
- 29. A method for inhibiting phosphotidylinositol (PI) 3-kinase activity in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound effective to inhibit phosphotidylinositol (PI) 3-kinase activity in the human or animal subject, wherein the compound has the formula I:

$$Y \xrightarrow{X} X \xrightarrow{R_1} R_2$$

$$X \xrightarrow{N} X \xrightarrow{N} N$$

$$W$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

(1) substituted or unsubstituted C_1 - C_6 -alkyl,

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- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and -N

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) $-NHR^{1t}$,

wherein R^{1t} is H or C₁-C₆-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

(3)
$$R^{4w} = \sum_{Z \cdot (CH_2)r}^{N},$$

wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R1w and

R^{2w} are not both H;

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^{z}$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and

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- (f) $-NHR^{5w}$, wherein R^{5w} is H or C_1 - C_6 -alkyl; and r is 0, 1, or 2.
- 30. A method for treating a cancer disorder in a human or animal subject, comprising administering to the human or animal subject a composition comprising an amount of a compound effective to inhibit phosphotidylinositol (PI) 3-kinase activity in the human or animal subject, wherein the compound has the formula I:

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and

$$(9) \qquad -N \bigcirc N - ,$$

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

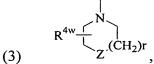
wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C₁-C₆-alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and



wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted aryl,

- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{lw} and R^{2w} are not both H;

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^{z}$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_2$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C₁-C₆-alkyl; and

r is 0, 1, or 2.

- 31. The method of Claim 30 further comprising administering to the human or animal subject at least one additional agent for the treatment of cancer.
- 32. The method of Claim 31, wherein the at least one additional agent for the treatment of cancer is selected from irinotecan, topotecan, gemcitabine, gleevec, herceptin, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, vinca alkaloids, imatinib, anthracyclines, rituximab, tamoxifen, CPT 11, and trastuzumab.
- 33. A method for inhibiting tumor growth in a human or animal subject, comprising administering to the human or animal subject in need thereof an effective amount of a compound having the formula I:

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$$Y \xrightarrow{X} \bigvee_{N = N}^{R_1} R_2$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) -SO₂-
- (8) $-C(R^{2x}, R^{3x})$ -, and -N

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,

- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and

R^{2w} are not both H;

(3)

Z is selected from the group consisting of

- (a) -O-,
- (b) -NRz-,
- (c) -S-,

- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_2$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.

34. A method for inhibiting the proliferation of capillaries in a human or animal subject, comprising administering to the human or animal subject in need thereof an effective amount of a compound having the formula I:

$$Y \xrightarrow{X} \begin{matrix} R_1 \\ N & N \end{matrix} \begin{matrix} R_2 \\ W \end{matrix}$$
(I)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

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X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and
- (9)

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

$$R^{4w}$$
 $C_{Z'}^{N}$ $C_{H_2}^{N}$

wherein R^{1w} and R^{2w} are selected from the group consisting of

(a) H,

(3)

R2w are not both H;

- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^{z}$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein Rz is H or substituted or unsubstituted alkyl group; and

 R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C₁-C₆-alkyl; and

r is 0, 1, or 2.

35. A compound for use in the treatment of cancer, wherein the compound has the formula I:

$$Y \xrightarrow{X} \bigvee_{N = N}^{R_1} R_2$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and
- (9)

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,

- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) -NHR^{1t},

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

$$R^{4w}$$
 $Z^{(CH_2)r}$

(3)

wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and

R2w are not both H;

Z is selected from the group consisting of

- (a) -O-
- (b) $-NR^{z}$ -,

- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein R^z is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.

34. A method for inhibiting the proliferation of capillaries in a human or animal subject, comprising administering to the human or animal subject in need thereof an effective amount of a compound having the formula I:

$$Y \xrightarrow{X} \xrightarrow{R_1} \xrightarrow{R_2} W$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and

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(6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})$ -,
- (3) $-(CH_2)_m-C(R^{2x}, R^{3x})-N(R^{1x})-$,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and -N

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H.
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,
- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- (e) substituted or unsubstituted aryl,
- (f) substituted or unsubstituted heterocyclyl,
- (g) substituted or unsubstituted heteroaryl; and

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) H,
- (2) substituted or unsubstituted C_1 - C_6 -alkyl,
- (3) -COOH,
- (4) halo,
- (5) $-OR^{1t}$, and
- (6) $-NHR^{1t}$,

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and

(3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) $-N(R^{1w}, R^{2w})$, and

$$R^{4w}$$
 $Z^{(CH_2)r}$

wherein R^{1w} and R^{2w} are selected from the group consisting of

(a) H,

(3)

- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) substituted or unsubstituted aryl,
- (d) substituted or unsubstituted heterocyclyl, and
- (e) substituted or unsubstituted heteroaryl, wherein R^{1w} and R^{2w} are not both H;

Z is selected from the group consisting of

- (a) -O-,
- (b) $-NR^{z}$ -,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_{2}$ -,

wherein Rz is H or substituted or unsubstituted alkyl group; and

R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.

36. Use of a compound in the manufacture of a medicament for the treatment of cancer, wherein the compound has the formula I:

$$Y \xrightarrow{X} \bigvee_{N = N}^{R_1} R_2$$

$$(I)$$

or a stereoisomer, tautomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein

Y is selected from the group consisting of

- (1) substituted or unsubstituted C_1 - C_6 -alkyl,
- (2) substituted or unsubstituted C₂-C₆-alkenyl,
- (3) substituted or unsubstituted C₂-C₆-alkynyl,
- (4) substituted or unsubstituted aryl,
- (5) substituted or unsubstituted heterocyclyl, and
- (6) substituted or unsubstituted heteroaryl;

X is selected from the group consisting of

- (1) a direct link,
- (2) $-N(R^{1x})-$,
- (3) $-(CH_2)_m$ - $C(R^{2x}, R^{3x})$ - $N(R^{1x})$ -,
- (4) -O-,
- (5) -S-,
- (6) -SO-,
- (7) $-SO_2$ -,
- (8) $-C(R^{2x}, R^{3x})$ -, and -N

(9) ,

wherein R^{1x}, R^{2x}, and R^{3x} are selected from the group consisting of

- (a) H
- (b) substituted or unsubstituted C₁-C₆-alkyl,
- (c) substituted or unsubstituted C₂-C₆-alkenyl,

- (d) substituted or unsubstituted C₂-C₆-alkynyl,
- substituted or unsubstituted aryl, (e)
- (f) substituted or unsubstituted heterocyclyl,
- substituted or unsubstituted heteroaryl; and (g)

m is 0, 1, 2, 3, or 4;

R₁ is selected from the group consisting of

- (1) Η,
- (2) substituted or unsubstituted C₁-C₆-alkyl,
- (3) -COOH,
- (4) halo,
- (5) -OR1t, and
- -NHR^{1t}, (6)

wherein R1t is H or C1-C6-alkyl;

R₂ is selected from the group consisting of

- (1) substituted or unsubstituted aryl,
- (2) substituted or unsubstituted heteroaryl, and
- (3) substituted or unsubstituted heterocyclyl; and

W is selected from the group consisting of

- substituted or unsubstituted C₁-C₆-alkyl, (1)
- $-N(R^{1w}, R^{2w})$, and (2) R^{4w} $(CH_2)r$

(3)

wherein R^{1w} and R^{2w} are selected from the group consisting of

- (a) Η,
- substituted or unsubstituted C₁-C₆-alkyl, (b)
- (c) substituted or unsubstituted aryl,
- substituted or unsubstituted heterocyclyl, and (d)
- substituted or unsubstituted heteroaryl, wherein R^{1w} and (e)

R²w are not both H;

Z is selected from the group consisting of

(a) -O-,

- (b) -NR^z-,
- (c) -S-,
- (d) -SO-,
- (e) $-SO_2$ -, and
- (f) $-CH_2-$,

wherein $R^{\text{\it z}}$ is H or substituted or unsubstituted alkyl group; and R^{4w} is selected from the group consisting of

- (a) H,
- (b) substituted or unsubstituted C_1 - C_6 -alkyl,
- (c) $-COOR^{5w}$,
- (d) $-CONH_2$,
- (e) $-OR^{5w}$, and
- (f) $-NHR^{5w}$,

wherein R^{5w} is H or C_1 - C_6 -alkyl; and

r is 0, 1, or 2.